1.0 PURPOSE

This policy is designed to ensure consistent and acceptable standards of expedited adverse event reporting to the Division of AIDS (DAIDS) by investigators participating in DAIDS funded and/or sponsored clinical trials.

2.0 SCOPE

This policy applies to DAIDS funded and/or sponsored clinical trials.

3.0 BACKGROUND

In the past, DAIDS has used several different serious adverse event (SAE) reporting manuals, reporting forms, and severity grading tables, depending on the type of study conducted. With the expansion of DAIDS international research, as well as the coordination of treatment, prevention, and vaccine research, the need to develop DAIDS-wide policies and procedures for expedited reporting of adverse events has been recognized and addressed. This policy is in accordance with US FDA and Office of Human Research Protections (OHRP) regulations, International Conference on Harmonisation (ICH) guidelines, National Institutes of Health (NIH) policy, and the National Institute of Allergy and Infectious Diseases (NIAID) Clinical Terms of Awards.

4.0 DEFINITIONS

Adverse Event (AE) – Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. In addition, if an untoward medical occurrence occurs as a result of study participation or study-related interventions, it is considered to be an adverse event.

Serious Adverse Event (SAE) – Any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. This includes important medical events that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the patient or may require intervention to prevent one of the outcomes listed in the definition above.

Expedited Adverse Event (EAE) – An adverse event that meets the criteria for expedited reporting, as specified in the Manual for Expedited Reporting of Adverse Events to DAIDS.

DAIDS Safety Office – The Office to which adverse events requiring expedited reporting are submitted. Currently located in the Regulatory Affairs Branch (RAB), Office for Policy in Clinical Research Operations (OPCRO) support contract and managed through RAB.

Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (AE Grading Table) – A list of common terms and severity (intensity) parameters used to describe adverse events occurring in DAIDS funded and/or sponsored clinical studies/trials.

Investigator of Record (IoR) – The person responsible for the conduct of the clinical trial at a clinical research site. This person is the signatory for the Form FDA 1572 (IND studies) or the DAIDS IoR Agreement (Non-IND studies). Written delegation of authority for specific trial responsibilities may be given to qualified individuals.

For additional definitions see DAIDS glossary.

5.0 RESPONSIBILITIES

In accordance with the US FDA Code of Federal Regulations and ICH guidelines, as the sponsor of a clinical trial, DAIDS is responsible for prompt and accurate reporting of any serious and unexpected (i.e., not listed in the investigator's brochure or package insert) adverse events associated with the use of a study agent to the FDA and to all investigators using the study agent in DAIDS funded and/or sponsored human subjects clinical trials.

The Investigator of Record conducting the DAIDS clinical trial is responsible for reporting all EAEs occurring at the clinical research site to the DAIDS Safety Office as soon as possible, and according to timeframes identified in the Manual for Expedited Reporting of Adverse Events to DAIDS.

6.0 POLICY

All DAIDS funded and/or sponsored clinical trials reviewed by the DAIDS Scientific Review Committees must use the current Manual for Expedited Reporting of Adverse Events to DAIDS (EAE Reporting Manual), the DAIDS Expedited Adverse Event (EAE) Form, and the DAIDS Table for Grading the Severity of

Adult and Pediatric Adverse Events (AE Grading Table) when reporting adverse events on an expedited basis. All adverse events that meet the criteria for expedited reporting to DAIDS must be submitted to the DAIDS Safety Office in English within the time period specified in the EAE Reporting Manual. However, ongoing studies supported or funded by DAIDS may continue use of legacy reporting systems until further notification by OPCRO.

The study protocol must specify which level of expedited adverse event reporting will be used, the study agents that will be considered in determining the relationship to any adverse events that occur, and the duration of the EAE reporting period. Additional reporting requirements may be added to the protocol on a case-by-case basis.

Any modification to these requirements must be approved in writing by the OPCRO Director or designee. Documentation of OPCRO approval will be available to DAIDS staff.

7.0 REFERENCES

International Conference on Harmonisation Guidance for Industry, Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (E2A)
http://www.ich.org/LOB/media/MEDIA436.pdf

International Conference on Harmonisation Guidance for Industry, Good Clinical Practice: Consolidated Guideline (E6)
http://www.ich.org/LOB/media/MEDIA482.pdf

Code of Federal Regulations, Title 21, Part 312
http://www.access.gpo.gov/nara/cfr/waisidx_05/21cfr312_05.html

NIAID Clinical Terms of Awards
http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf

DAIDS Expedited Adverse Event Reporting Materials (EAE Reporting Manual, Forms, AE Grading Table, guidance, and template protocol language).
http://rcc.tech-res-intl.com/eae.htm

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at:

NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL:
http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

The signed original is maintained in the OPCRO policy office.

10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
1.0	14 JUL 06	N/A	N/A	N/A

11.0 APPENDICES

The following materials are available for download at the DAIDS Safety Office website: http://rcc.tech-res-intl.com/eae.htm

- Manual for Expedited Reporting of Adverse Events to the DAIDS
- DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events
- DAIDS Expedited Adverse Event (EAE) Form
- Completion Instructions for the DAIDS EAE Form
- Template Wording for the Expedited Adverse Event Reporting Section of DAIDS-Sponsored Protocols

12.0 APPROVAL

	Signature	Program/Branch	Date
Authorized By:	Richard Hafner Richard Hafner, MD Director	Office for Policy in Clinical Research Operations	July 14, 2006